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EXAMINER	
CHEN, SHIN LIN	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/635,818	HARRINGTON ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-27* is/are pending in the application.

4a) Of the above claim(s) *12-21 and 23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11,22,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2-17-04, 5-24-04 and 7-29-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 2-11, 22, 26 and 27, in the reply filed on 11-5-07 is acknowledged.

2. Claims 12-21 and 23-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11-5-07.

Applicants' preliminary amendment filed on 2-2-04 has been entered. Claim 1 has been canceled. Claims 2-27 have been added. The abstract filed on 6-3-05 has been entered.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because there is no sequence identifier for the nucleotide sequence in Figures 29-35 and 37 or in the "BRIEF DESCRIPTION OF THE DRAWINGS". Each nucleotide sequence is required to have a sequence identifier. Appropriate correction is required.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 2-17-04, 5-24-04 and 7-29-04 were filed before the mailing of restriction requirement on 9-4-07. The submission is in

compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

4. Claim 2 is objected to because of the following informalities: the term "vectorcomprising" in claim 2 appears to be a typographical error. Appropriate correction is required.

5. Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 depends from claim 4. The eukaryotic cell in claim 4 is in vitro, which is considered "isolated". Therefore, claim 11 fails to further limit the subject matter of claim 4.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2-11, 22, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "the selectable marker **and/or** the unpaired splice donor" in claims 2, 3 and 22 is vague and renders the claims indefinite. It is unclear what is intended in the claims.

Changing the phrase to "the selectable marker or the unpaired splice donor or both" would be remedial.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 2-11, 22, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating a fusion transcript by non-homologous integration into the genome of an eukaryotic cell via splicing of a splice donor into a splice acceptor, does not reasonably provide enablement for generating a fusion transcript by non-homologous integration into the genome of an eukaryotic cell without splicing of a splice donor into a splice acceptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims

While determining whether a specification is enabling, one considered whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirement, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of

ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d at 737, 8 USPQ2d 1400, 1404 (Fed. Cir.1988)).

Furthermore, the USPTO does not have laboratory facilities to test if an invention with function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raises and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

Claims 2-11, 22, 26 and 27 are directed to a eukaryotic cell in vitro comprising a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said vector non-homologously integrated into the genome of said eukaryotic cell to generate a fusion transcript comprising the nucleotide sequence encoding the selectable marker and/or the splice donor and one or more exons of an endogenous gene under the control of the first or second promoter, and said endogenous sequence is translated, said vector, and a library of said eukaryotic cells in vitro. Claims 4-11 specify the eukaryotic cells is an animal cell, a mammalian cell, an insect cell, an avian cell, an annelid cell, a fish cell, a human cell, a plant cell, a fungal cell, and a yeast cell etc.

The claims encompass generating a fusion transcript comprising the nucleotide sequence encoding the selectable marker or the splice donor or both said nucleotide sequence and said splice donor, each with one or more exons of an endogenous gene by non-homologous

integration of a vector into the genome of a eukaryotic cell, and said fusion transcript is translated. The specification fails to provide adequate guidance and evidence for how to generate a fusion transcript comprising a nucleotide sequence encoding a selectable marker and one or more exons of an endogenous gene in the genome of a eukaryotic cell by non-homologous integration of a vector into said genome without the use of splice donor and splice acceptor. It was known in the art that retroviral DNA can integrate into genome of a cell non-homologously. Daniel et al., 2004 (Journal of Virology, Vol. 78, No. 16, p. 8573-8581) reports that cellular DNA repair system plays a role in completion of the retroviral DNA integration process. Cellular proteins involved in the non-homologous end joining (NHEJ) pathway, such as DNA-PKcs, Xrcc4 and ligase IV, are required for completion of the retroviral DNA integration process (e.g. abstract). However, the state of the art shows that a vector other than retroviral vector cannot non-homologously integrate into a genome of a eukaryotic cell without the presence of a splice donor and a splice acceptor. For example, a plasmid vector cannot non-homologously integrate into a genome of a eukaryotic cell without the presence of a splice donor and a splice acceptor. Even the retroviral vector requires the presence of cellular proteins involved in the NHEJ pathways for non-homologous integration into genome. Absent specific guidance and evidence, one skilled in the art at the time of the invention would not know how to generate a fusion transcript comprising a nucleotide sequence encoding a selectable marker and one or more exons of an endogenous gene in the genome of a eukaryotic cell by non-homologous integration of a vector into said genome without the use of splice donor and splice acceptor.

For the reasons set forth above, one skilled in the art at the time of the invention would have to engage in undue experimentation to practice over the full scope of the invention claimed.

This is particularly true based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, the level of skill which is high, the amount of experimentation required, and the breadth of the claims.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 2-11 and 22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-9, 11 and 12 of U.S. Patent No. 7,033,782 ('782). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 2-11 and 22 of the instant invention are directed to a eukaryotic cell in vitro comprising a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said vector non-homologously integrated into the genome of said eukaryotic cell to generate a fusion transcript comprising the nucleotide sequence encoding the selectable marker and/or the splice donor and one or more exons of an endogenous gene under the control of the first or second promoter, and said endogenous sequence is translated, and a library of said eukaryotic cells in vitro. Claims 4-11 specify the eukaryotic cells is an animal cell, a mammalian cell, an insect cell, an avian cell, an annelid cell, a fish cell, a human cell, a plant cell, a fungal cell, and a yeast cell etc.

Claims 7-9, 11 and 12 of '782 are directed to a purified eukaryotic cell expressing a protein, the genome of said cell comprising a genetically engineered vector comprising a transcriptional regulatory sequence operably linked to a splice donor sequence and said regulatory sequence is operably linked to an endogenous gene encoding said protein, the splice donor sequence being spliced to a splice acceptor sequence in said gene, and the genetically engineered vector is inserted into said gene non-homologously. Claim 8 specifies the vector additionally contains an amplifiable marker.

The eukaryotic cell of the instant invention encompasses eukaryotic cells producing fusion transcript comprising a nucleotide sequence encoding a selectable marker or a splice donor under the control of a promoter or both said nucleotide sequence and said splice donor, each with one or more exons of an endogenous gene by non-homologous integration of a vector into the genome of a eukaryotic cell. The eukaryotic cell in '782 encompasses those eukaryotic

cells recited in the instant invention. Although '782 does not specifically mention a selectable marker, however, claim 8 specifies the vector contains an amplifiable marker, which can be interpreted as a selectable marker. Further, it would be obvious for one of ordinary skill in the art to add a selectable marker in the claimed vector because it is general practice to use a selectable marker to identify a transfected cell from non-transfected cell. A transcriptional regulatory sequence encompasses a promoter sequence. Preparation of the claimed purified eukaryotic cell of '782 would produce a library of said eukaryotic cell. Thus, claims 2-11 and 22 would be obvious to one of ordinary skill in the art at the time of the invention in view of claims 7-9, 11 and 12 of '782.

12. Claims 2-11 and 22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 6,740,503 ('503). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 2-11 and 22 of the instant invention are directed to a eukaryotic cell in vitro comprising a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said vector non-homologously integrated into the genome of said eukaryotic cell to generate a fusion transcript comprising the nucleotide sequence encoding the selectable marker and/or the splice donor and one or more exons of an endogenous gene under the control of the first or second promoter, and said

endogenous sequence is translated, and a library of said eukaryotic cells in vitro. Claims 4-11 specify the eukaryotic cells is an animal cell, a mammalian cell, an insect cell, an avian cell, an annelid cell, a fish cell, a human cell, a plant cell, a fungal cell, and a yeast cell etc.

Claim 10 of '503 is directed to a host cell comprising a vector comprising (a) a promoter operably linked to an exon and a splice donor site at the 3' end of the exon, (b) one or more selectable markers which lacks a polyadenylation signal, (c) one or more viral origins of replication, and (d) a genomic DNA fragment, wherein said promoter, exon and splice donor are operably linked to a gene or portion thereof in said genomic DNA fragment, wherein said exon and/or protmoer is heterologous to said gene or portion thereof in said genomic DNA fragment, and the splice donor is spliced to a splice acceptor on the genomic DNA fragment to produce a transcript, which is translated.

The eukaryotic cell of the instant invention encompasses eukaryotic cells producing fusion transcript comprising a nucleotide sequence encoding a selectable marker or a splice donor under the control of a promoter or both said nucleotide sequence and said splice donor, each with one or more exons of an endogenous gene by non-homologous integration of a vector into the genome of a eukaryotic cell. The host cell in '503 encompasses those eukaryotic cells recited in the instant invention. Preparation of the claimed host cell of '503 would produce a library of the eukaryotic cell of the instant invention. Thus, claims 2-11 and 22 would be obvious to one of ordinary skill in the art at the time of the invention in view of claim 10 of '503.

13. Claims 2-11, 22, 26 and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 11, 13, 19 and 20 of U.S. Patent No.

6,623,958 ('958, IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 2-11, 22, 26 and 27 of the instant invention are directed to a eukaryotic cell in vitro comprising a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said vector non-homologously integrated into the genome of said eukaryotic cell to generate a fusion transcript comprising the nucleotide sequence encoding the selectable marker and/or the splice donor and one or more exons of an endogenous gene under the control of the first or second promoter, and said endogenous sequence is translated, said vectors, and a library of said eukaryotic cells in vitro. Claims 4-11 specify the eukaryotic cells is an animal cell, a mammalian cell, an insect cell, an avian cell, an annelid cell, a fish cell, a human cell, a plant cell, a fungal cell, and a yeast cell etc.

Claims 1, 3, 4, 11, 13, 19 and 20 of '958 are directed to a vector comprising a first promoter, a sequence encoding a positive selectable marker, a sequence encoding a negative selectable marker, and an unpaired splice donor site, wherein when said vector is integrated into a genome of a eukaryotic cell, the splice donor is spliced to a splice acceptor in the host cell genome and said positive selectable marker is expressed in active form and said negative selectable marker is not expressed or is expressed in inactive form, a eukaryotic host cell in vitro comprising said vector, and a library of eukaryotic host cells in vitro comprising said vector. Claim 3 specifies the positive or negative or both selectable markers lack a polyadenylation

signal. Claim 4 specifies the vector further comprises a second promoter operably linked to a second unpaired splice donor site. Claim 11 recites various positive selectable markers, such as neomycin gene and puromycin gene etc.

The eukaryotic cell of the instant invention encompasses eukaryotic cells producing fusion transcript comprising a nucleotide sequence encoding a selectable marker or a splice donor under the control of a promoter or both said nucleotide sequence and said splice donor, each with one or more exons of an endogenous gene by non-homologous integration of a vector into the genome of a eukaryotic cell. The eukaryotic host cell of '958 encompasses those eukaryotic cells recited in the instant invention. Thus, claims 2-11, 22, 26 and 27 would be obvious to one of ordinary skill in the art at the time of the invention in view of claims 1, 3, 4, 11, 13, 19 and 20 of '958.

14. Claims 2-11, 22, 26 and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7, 8, 10-13, 16, 18, 19 and 21-28 of U.S. Patent No. 6,602,686 ('686, IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 2-11, 22, 26 and 27 of the instant invention are directed to a eukaryotic cell in vitro comprising a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said vector non-homologously integrated into the genome of said eukaryotic cell to generate a fusion transcript

comprising the nucleotide sequence encoding the selectable marker and/or the splice donor and one or more exons of an endogenous gene under the control of the first or second promoter, and said endogenous sequence is translated, said vectors, and a library of said eukaryotic cells in vitro. Claims 4-11 specify the eukaryotic cells is an animal cell, a mammalian cell, an insect cell, an avian cell, an annelid cell, a fish cell, a human cell, a plant cell, a fungal cell, and a yeast cell etc.

Claims 1-4, 7, 8, 10-13, 16, 18, 19 and 21-28 of '686 are directed to a vector comprising a first promoter operably linked to an exon defined at the 3' end by an unpaired splice donor sequence, and a second promoter operably linked to an exon defined at the 3' end by an unpaired splice donor sequence, wherein the exon sequence is derived from a naturally occurring eukaryotic gene or is synthetic, a eukaryotic cell in vitro produced by introducing the vector into said eukaryotic cell wherein said vector is non-homologously integrated into the genome of said eukaryotic cell in such a way that a fusion transcript comprising said first unpaired splice donor sequence and/or said second unpaired splice donor sequence of the vector and one or more exons of an endogenous gene is expressed under the control of said first or said second promoter and coding sequence in said endogenous gene is translated, and a library of eukaryotic cells in vitro comprising said vector. Claims 23-26 specify various eukaryotic cells.

The eukaryotic cell of the instant invention encompasses eukaryotic cells producing fusion transcript comprising a nucleotide sequence encoding a selectable marker or a splice donor under the control of a promoter or both said nucleotide sequence and said splice donor, each with one or more exons of an endogenous gene by non-homologous integration of a vector into the genome of a eukaryotic cell. The exon of the vector in '686 could be a selectable marker

lacking a polyadenylation signal and would be obvious to one of ordinary skill in the art because the eukaryotic cell in claims 7 and 8 requires expression of a fusion transcript comprising said first unpaired splice donor sequence and/or said second unpaired splice donor sequence and one or more exons of an endogenous gene, and said transcript is translated to produce a protein. Although '686 does not specifically mention a selectable marker, however, claim 16 specifies the vector contains one or more amplifiable markers, which can be interpreted as a selectable marker. Further, it would be obvious for one of ordinary skill in the art to add a selectable marker in the claimed vector because it is general practice to use a selectable marker to identify a transfected cell from non-transfected cell. Thus, claims 2-11, 22, 26 and 27 would be obvious to one of ordinary skill in the art at the time of the invention in view of claims 1-4, 7, 8, 10-13, 16, 18, 19 and 21-28 of '686.

15. Claims 2-11 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 92-99 and 110-116 of copending Application No. 10/331,329 ('329, IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 2-11 and 22 of the instant invention are directed to a eukaryotic cell in vitro comprising a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said vector non-homologously integrated into the genome of said eukaryotic cell to generate a fusion transcript comprising the

nucleotide sequence encoding the selectable marker and/or the splice donor and one or more exons of an endogenous gene under the control of the first or second promoter, and said endogenous sequence is translated, and a library of said eukaryotic cells in vitro. Claims 4-11 specify the eukaryotic cells is an animal cell, a mammalian cell, an insect cell, an avian cell, an annelid cell, a fish cell, a human cell, a plant cell, a fungal cell, and a yeast cell etc.

Claims 92-99 and 110-116 of '329 are directed to a eukaryotic cell in vitro comprising in its genome a vector comprising a transcriptional regulatory sequence operably linked to an unpaired splice donor sequence and one or more sequence encoding an amplifiable marker, wherein said vector does not comprise a homologous targeting sequence. The transcriptional regulatory sequence can be a promoter, such as a viral promoter, a CMV promoter, and the eukaryotic cell can be a mammalian cell.

The eukaryotic cell of the instant invention encompasses eukaryotic cells producing fusion transcript comprising a nucleotide sequence encoding a selectable marker or a splice donor under the control of a promoter or both said nucleotide sequence and said splice donor, each with one or more exons of an endogenous gene by non-homologous integration of a vector into the genome of a eukaryotic cell. The eukaryotic cell in '329 encompasses those eukaryotic cells recited in the instant invention. Although '329 does not specifically mention a selectable marker, however, the vector of '329 contains one or more sequence encoding an amplifiable marker, which can be interpreted as a selectable marker. Further, it would be obvious for one of ordinary skill in the art to add a selectable marker in the claimed vector because it is general practice to use a selectable marker to identify a transfected cell from non-transfected cell. Preparation of the claimed eukaryotic cell of '329 would produce a library of said eukaryotic

cell. Thus, claims 2-11 and 22 would be obvious to one of ordinary skill in the art at the time of the invention in view of claims 92-99 and 110-116.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Applicant is advised that should claim 2 be found allowable, claim 3 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claim 27 is rejected under 35 U.S.C. 102(e) as being anticipated by Burgess et al., 2000 (US Patent No. 6,139,833).

Claim 27 is directed to a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal,

and (ii) a second promoter operably linked to an unpaired splice donor, wherein said selectable marker is puromycin or neomycin etc.

Burgess teaches preparation of a vector, such as VICTR3, VICTR6 and VICTR7, which comprises a PGK promoter operably linked to a puromycin gene without polyadenylation signal and a splice donor (SD) sequence operably linked to a LTR containing U5, R and U3 (e.g. Figure 2, column 20). Thus, claim 27 is anticipated by Burgess.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Burgess et al., 2000 (US Patent No. 6,139;833).

Claim 26 is directed to a vector comprising (i) a first promoter operably linked to a nucleotide sequence encoding a selectable marker but lacks a functional polyadenylation signal, and (ii) a second promoter operably linked to an unpaired splice donor, wherein said promoter is selected from the group consisting of a CMV promoter, a SV40 T antigen promoter, a tetracycline-inducible promoter, and a beta-actin promoter.

Burgess teaches preparation of a vector, such as VICTR3, VICTR6 and VICTR7, which comprises a PGK promoter operably linked to a puromycin gene without polyadenylation signal and a splice donor (SD) sequence operably linked to a LTR containing U5, R and U3 (e.g. Figure 2).

Burgess does not specifically teach using CMV promoter or SV40 promoter etc.

It would have been prima facie obvious for one of ordinary skill in the art at the time of the invention to use CMV promoter or SV40 promoter etc. for the vector as claimed because Burgess teaches using mouse phosphoglycerate kinase (PGK) promoter for the VICTR3 vector and suggests that any appropriate promoter that are known to be active in a given cell type may be used for the VICTR vectors. Since the recited promoters, such as CMV promoter and SV40 promoter, are well known in the art, therefore, it would be obvious for one of ordinary skill to use the recited promoter for the claimed vector of the instant invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to express the selectable marker, such as puromycin, as taught by Burgess with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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PRIMARY EXAMINER